	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	2208	thrombin adj inhibitor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:44			0
2	BRS	L2	143	(thrombin adj inhibitor) same prodrug	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:45			0
3	BRS	L3	1887347	kit or composition	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:45			0
4	BRS	L4	6	2 same 3	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:45			0
5	BRS	L5	38	melagatran	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:52			0
6	BRS	L6	13	melagatran same prodrug	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:52			0
7	BRS	L7	4	(melagatran same prodrug) same (kit or composition)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:55			0
8	BRS	L8	0	thrombotic adj condtion	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:55			0
9	BRS	L9	22723	thrombosis	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:55			0
10	BRS	L10	1	9 same (6 or 4)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:57			0
11	BRS	L11	93918	surgery	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:56			0
12	BRS	L12	2592	9 same 11	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:56			0

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(FILE 'HOME' ENTERED AT 15:02:44 ON 27 MAY 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
15:03:08 ON 27 MAY 2003
L1 10904 S THROMBIN INHIBITOR
L2 514 S MELAGATRAN
L3 11005 S L1 OR L2
L4 68 S L3 (P) PRODRUG
L5 2981974 S KIT OR COMPOSITION
L6 0 S L4 (P) L5
L7 263691 S THROMBOSIS
L8 277 S THROMBOTIC CONDITION
L9 263784 S L7 OR L8
L10 13 S L9 (P) L4
L11 8 DUPLICATE REMOVE L10 (5 DUPLICATES REMOVED)
L12 21370 S L9 (P) SURGERY
L13 3 S L11 (P) L12
L14 0 S L13 NOT L11

=> log y

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
13	BRS	L13	0	12 same (6 or 4)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:57			0
14	BRS	L14	15	gustafsson adj david.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:59			0
15	BRS	L15	1	14 and (6 or 4)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/27 14:59			0

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FILE 'HOME' ENTERED AT 15:02:44 ON 27 MAY 2003

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 15:03:08 ON 27 MAY 2003

FILE 'CAPLUS' ENTERED AT 15:03:08 ON 27 MAY 2003
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FILE 'BIOSIS' ENTERED AT 15:03:08 ON 27 MAY 2003
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FILE 'EMBASE' ENTERED AT 15:03:08 ON 27 MAY 2003
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FILE 'SCISEARCH' ENTERED AT 15:03:08 ON 27 MAY 2003
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FILE 'AGRICOLA' ENTERED AT 15:03:08 ON 27 MAY 2003

=> s thrombin inhibitor
L1        10904 THROMBIN INHIBITOR

=> s melagatran
L2          514 MELAGATRAN

=> s l1 or l2
L3        11005 L1 OR L2

=> s l3 (p) prodrug
L4           68 L3 (P) PRODRUG

=> s kit or composition
L5      2981974 KIT OR COMPOSITION

=> s l4 (p) l5
L6            0 L4 (P) L5

=> s thrombosis
L7       263691 THROMBOSIS

=> s thrombotic condition
L8          277 THROMBOTIC CONDITION

=> s l7 or l8
L9       263784 L7 OR L8

=> s l9 (p) l4
L10          13 L9 (P) L4

=> duplicate remove l10
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L10
L11            8 DUPLICATE REMOVE L10 (5 DUPLICATES REMOVED)

=> d l11 1-8 ibib abs

L11  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2002:879541  CAPLUS
DOCUMENT NUMBER:          137:362345
TITLE:                    Oral-direct thrombin inhibitors
AUTHOR(S):                Crowther, Mark A.
CORPORATE SOURCE:         McMaster University, Hamilton, ON, Can.
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SOURCE: Fundamental and Clinical Cardiology (2003), 46(New Therapeutic Agents in Thrombosis and Thrombolysis (2nd Edition)), 265-271
CODEN: FCCAEH; ISSN: 1067-5264
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Current strategies for the treatment and prevention of venous ***thrombosis*** require a mix of parenteral and oral therapies that frequently require lab. monitoring. Oral-direct ***thrombin*** ***inhibitors*** have the potential to simplify antithrombotic therapy; these agents produce a predictable anticoagulant response so that lab. monitoring may be unnecessary. Ximelagatran, the oral direct ***thrombin*** ***inhibitor*** in the most advanced stage of development, is a ***prodrug*** of ***melagatran*** , an active-site-directed inhibitor of thrombin. In phase II studies, ximelagatran has been evaluated as thromboprophylaxis in patients undergoing elective hip or knee replacement surgery and in patients with nonvalvular atrial fibrillation. The drug has also been studied in patients with acute venous ***thrombosis*** . In each case, ximelagatran appears to be at least as safe and effective as current antithrombotic interventions. Phase III studies with ximelagatran for these indications are currently underway. If ximelagatran lives up to its initial promise, it has the potential to revolutionize the prevention and treatment of ***thrombosis*** .

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 8 MEDLINE
ACCESSION NUMBER: 2002416506 MEDLINE
DOCUMENT NUMBER: 22161009 PubMed ID: 12170516
TITLE: [Prophylaxis of postoperative thromboembolism. New alternatives to low-molecular-weight heparin]. Profylax mot postoperativ tromboembolism. Nya alternativ till lagmolekylart heparin.
AUTHOR: Bergqvist David; Siegbahn Agneta
CORPORATE SOURCE: Avdelningen for klinisk kemi, Akademiska sjukhuset, Uppsala.. david.bergqvist@kirurgi.uu.se
SOURCE: LAKARTIDNINGEN, (2002 Jul 11) 99 (28-29) 3039-41.
Journal code: 0027707. ISSN: 0023-7205.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Swedish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020813
Last Updated on STN: 20020914
Entered Medline: 20020913

AB For somewhat more than a decade low molecular weight heparins have dominated in the pharmacological prevention of postoperative venous thromboembolism. At present there are some new methods of potential interest both as prophylactic substances but also to better understand the pathophysiology of deep vein ***thrombosis*** . These are inhibition of factor VII a/tissue factor complex (NAP, Nematode Anticoagulant Protein), inhibition of activated factor X (the synthetic pentasaccharide fondaparinux) and thrombin inhibition (***melagatran*** and its oral ***prodrug*** ximelagatran). They have been shown to be effective in high risk orthopaedic surgery. They have to show their place in the prophylactic arsenal in comparison with low molecular weight heparins (effect, safety, mode of administration, cost-effectiveness).

L11 ANSWER 3 OF 8 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002388952 MEDLINE
DOCUMENT NUMBER: 22132572 PubMed ID: 12137410
TITLE: BIBR-1048 Boehringer Ingelheim.
AUTHOR: Mungall Dennis
CORPORATE SOURCE: The Miami Project to Cure Paralysis, Department of Neurological Surgery, University of Miami School of Medicine, Lois Pope Life Center, FL 33101, USA.. Thertch@aol.com
SOURCE: Curr Opin Investig Drugs, (2002 Jun) 3 (6) 905-7. Ref: 13
Journal code: 100965718. ISSN: 1472-4472.

PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20020725
Last Updated on STN: 20030227
Entered Medline: 20030226

AB BIBR-1048, a ***thrombin*** ***inhibitor*** and an orally-active ***prodrug*** of BIBR-953ZW, is under development by Boehringer Ingelheim as a potential antithrombotic agent [331881]. By 1999, BIBR-1048 was in phase II clinical trials for thromboembolism and the prevention of stroke due to atrial fibrillation [331881]; by April 2002, proof-of-principle had been demonstrated in phase II trials in deep vein ***thrombosis*** [446554]. In July 2001, the company revealed that an IND was expected to be filed for BIBR-953ZW in 2002 [415884].

L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:154081 CAPLUS
TITLE: Mechanisms of action and principal pharmacological properties of the new antithrombotic agents
AUTHOR(S): Samama, M. M.; Gerotziafas, G. T.
CORPORATE SOURCE: Service d'hematologie biologique, Hotel-Dieu, Paris, 75004, Fr.
SOURCE: Lettre du Pharmacologue (2002), 16(6), 154-160
CODEN: LPEHAV; ISSN: 0984-452X
PUBLISHER: Edimark S.A. (Vivactis Media)
DOCUMENT TYPE: Journal
LANGUAGE: French

AB Fondaparinux (Arixtra) and ximelagatran (Exanta) represent a real innovation for the prevention and treatment of deep vein ***thrombosis*** . They are completely synthetic and specific inhibitors of a unique serine protease of blood coagulation. Fondaparinux is the first of a new class of selective antithrombin dependent indirect factor Xa inhibitors, which inhibit thrombin generation. Ximelagatran, the ***prodrug*** of ***melagatran*** , is a unique new antithrombotic drug, since it is the first clin. used direct orally acting reversible ***thrombin*** ***inhibitor*** . This review summarizes the history of pentasaccharide and ximelagatran, their mol. structures, their mechanism of action and their pharmacokinetics.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:851154 CAPLUS
DOCUMENT NUMBER: 135:371637
TITLE: Synthesis of thiochromane derivatives for use as thrombin inhibitors
INVENTOR(S): Andersson, Kjell; Inghardt, Tord; Karlsson, Olle; Linschoten, Marcel; Nystroem, Jan-erik; Sunden, Gunnel
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087879	A1	20011122	WO 2001-SE1052	20010514

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1283837 A1 20030219 EP 2001-930400 20010514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
NO 2002005504 A 20021115 NO 2002-5504 20021115
PRIORITY APPLN. INFO.: SE 2000-1803 A 20000516
WO 2001-SE1052 W 20010514
OTHER SOURCE(S): MARPAT 135:371637
GI

/ Structure 1 in file .gra /

AB Synthesis of thiochromane derivs. (I) (R1 = halo; R2 = H, halo, alkoxy; Y = S=O, SO2) for use as ***thrombin*** ***inhibitors*** is disclosed. Thus, I (R1 = Cl, R2 = H, Y = SO2) (II) is prepd. in 8 steps from 4-chloro-2-methoxythiophenol, Et bromopropanoate and paraamidinobenzylamino azetidinecarboxylate. II in thrombin clotting time assay shows an IC50TT of > 0.05.upsilon.M. I are useful as ***prodrugs*** , competitive inhibitors of trypsinlike proteases, such as thrombin, and in particular in the treatment of conditions where inhibitors of thrombin is required (e.g. ***thrombosis***) or as anticoagulants.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 8 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001301777 MEDLINE
DOCUMENT NUMBER: 21127175 PubMed ID: 11228340
TITLE: The direct thrombin inhibitor melagatran and its oral prodrug H 376/95: intestinal absorption properties, biochemical and pharmacodynamic effects.
AUTHOR: Gustafsson D; Nystrom J; Carlsson S; Bredberg U; Eriksson U; Gyzander E; Elg M; Antonsson T; Hoffmann K; Ungell A; Sorensen H; Nagard S; Abrahamsson A; Bylund R
CORPORATE SOURCE: Department of Cardiovascular Pharmacology, AstraZeneca R&D Molndal, S-431 83, Molndal, Sweden..
david.gustafsson@astrazeneca.com
SOURCE: THROMBOSIS RESEARCH, (2001 Feb 1) 101 (3) 171-81.
Journal code: 0326377. ISSN: 0049-3848.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010604
Last Updated on STN: 20030314
Entered Medline: 20010531
AB Suboptimal gastrointestinal absorption is a problem for many direct ***thrombin*** ***inhibitors*** . The studies presented herein describe the new oral direct ***thrombin*** ***inhibitor*** H 376/95, a ***prodrug*** with two protecting residues added to the direct ***thrombin*** ***inhibitor*** ***melagatran*** . Absorption properties in vitro: H 376/95 is uncharged at intestinal pH while ***melagatran*** is charged. H 376/95 is 170 times more lipophilic (octanol water partition coefficient) than ***melagatran*** . As a result, the permeability coefficient across cultured epithelial Caco-2 cells is 80 times higher for H 376/95 than for melagtran. Pharmacokinetic studies in healthy volunteers: H 376/95 is converted to ***melagatran*** in man. Oral bioavailability, measured as ***melagatran*** in plasma, is about 20% after oral administration of H 376/95, which is 2.7-5.5 times higher than after oral administration of ***melagatran*** . The variability in the area under the drug plasma concentration vs. time curve (AUC) is much smaller with oral H 376/95 (coefficient of variation 20%) than with oral ***melagatran*** (coefficient of variation 38%). Pharmacodynamic properties: H 376/95 is inactive towards human alpha-thrombin compared with ***melagatran*** [inhibition constant (K(i)) ratio, 185 times], a potential advantage for patients with silent gastrointestinal bleeding. In an experimental ***thrombosis*** model in the rat, oral H 376/95 was more effective than the subcutaneous low molecular weight heparin dalteparin in preventing ***thrombosis*** . Conclusion: By the use of the ***prodrug***

principle, H 376/95 endows the direct ***thrombin*** ***inhibitor*** ***melagatran*** with pharmacokinetic properties required for oral administration without compromising the promising pharmacodynamic properties of ***melagatran*** .

L11 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:772474 CAPLUS
DOCUMENT NUMBER: 133:340244
TITLE: A pharmaceutical formulation comprising a low molecular weight thrombin inhibitor and its prodrug
INVENTOR(S): Gustafsson, David
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064470	A1	20001102	WO 2000-SE756	20000419
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
SE 9901442	A	20001022	SE 1999-1442	19990421
BR 2000009847	A	20020108	BR 2000-9847	20000419
EP 1200118	A1	20020502	EP 2000-928047	20000419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
AU 754405	B2	20021114	AU 2000-46336	20000419
JP 2002542298	T2	20021210	JP 2000-613460	20000419
EE 200100543	A	20030217	EE 2001-543	20000419
NO 2001005107	A	20011019	NO 2001-5107	20011019

PRIORITY APPLN. INFO.: SE 1999-1442 A 19990421
SE 1999-4419 A 19991203
WO 2000-SE756 W 20000419
OTHER SOURCE(S): MARPAT 133:340244
AB A pharmaceutical formulation contains a low mol. wt. ***thrombin*** ***inhibitor*** , or a pharmaceutically acceptable deriv. with an adjuvant, diluent or carrier; a pharmaceutical formulation including a ***prodrug*** of a low mol. wt. ***thrombin*** ***inhibitor*** , or a deriv. of that ***prodrug*** , in admixt. with an adjuvant, diluent or carrier. The formulation is suitable for administration in the treatment of a condition in which the inhibition of thrombin is required. A controlled, randomized, parallel group, Swedish multi-center pilot study was carried out. The study was open with regard to the drugs under evaluation but was blind for the patients, all personnel at the study sites, and for the person monitoring the expts. with regard to the doses of ***melagatran*** and the ***prodrug*** of ***melagatran*** , EtOOC-CH2-(R)Cgl-Aze-Pab-OH (I). A combination of s.c. administered ***melagatran*** and orally administered I is effective in preventing venous ***thrombosis*** after orthopedic surgery.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:506597 CAPLUS
DOCUMENT NUMBER: 127:136080
TITLE: Preparation of peptide derivatives as prodrugs of thrombin inhibitors
INVENTOR(S): Antonsson, Thomas; Gustafsson, David; Hoffmann, Kurt-Jurgen; Nystrom, Jan-Erik; Sorensen, Henrik; Sellen, Mikael
PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.; Antonsson, Thomas; Gustafsson, David; Hoffmann, Kurt-Jurgen; Nystrom,

SOURCE: Jan-Erik; Sorensen, Henrik; Sellen, Mikael
PCT Int. Appl., 94 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9723499	A1	19970703	WO 1996-SE1680	19961217
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9610353	A	19970623	ZA 1996-10353	19961209
CA 2238737	AA	19970703	CA 1996-2238737	19961217
AU 9712178	A1	19970717	AU 1997-12178	19961217
AU 706350	B2	19990617		
EP 869966	A1	19981014	EP 1996-943446	19961217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1209139	A	19990224	CN 1996-180024	19961217
BR 9612148	A	19990713	BR 1996-12148	19961217
JP 2000504313	T2	20000411	JP 1997-523571	19961217
JP 3282821	B2	20020520		
EP 995755	A1	20000426	EP 1999-120315	19961217
EP 995755	B1	20010816		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 324902	A	20000623	NZ 1996-324902	19961217
JP 2001089498	A2	20010403	JP 2000-220423	19961217
AT 204292	E	20010915	AT 1999-120315	19961217
RU 2176644	C2	20011210	RU 1998-111148	19961217
ES 2163916	T3	20020201	ES 1999-120315	19961217
EE 4022	B1	20030415	EE 1998-187	19961217
US 5965692	A	19991012	US 1997-776231	19970131
NO 9802809	A	19980820	NO 1998-2809	19980618
US 6262028	B1	20010717	US 1999-353644	19990715
HK 1026214	A1	20020809	HK 2000-105419	20000830
US 2002142968	A1	20021003	US 2002-74008	20020214

PRIORITY APPLN. INFO.:

GB 1995-26273	A	19951221
SE 1996-556	A	19960215
EP 1996-943446	A3	19961217
JP 1997-523571	A3	19961217
WO 1996-SE1680	W	19961217
US 1997-776231	A1	19970131
US 1999-353644	A1	19990715
US 2000-708449	B1	20001109

OTHER SOURCE(S): MARPAT 127:136080

AB Title compds. of formula R1O(O)C-CH2-(R)Cgl-Aze-Pab-R2 [wherein R1 = H, C1-10 alkyl, (un)substituted C1-3 alkylphenyl, A1C(O)N(R3)R4, A1C(O)OR3; (R)Cgl = (R)-cyclohexyl glycine; Aze = (S)-azetidine-2-carboxylic acid; Pab = 1-amidino-4-aminomethylbenzene; R2 (which replaces one of the hydrogen atoms in the amidino unit of Pab) = OH, OC(O)R5, C(O)OR6, C(O)OCH(R7)OC(O)R8; R3 and R4 are independently e.g., H, C1-6 alkyl, Ph, or together with the nitrogen atom represent pyrrolidinyl or piperidinyl; R5 = C1-17 alkyl, Ph, or 2-naphthyl (all of which are optionally substituted by C1-6 alkyl or halogen); R6 = (un)substituted 2-naphthyl, Ph, C1-3 alkylphenyl, C1-12 alkyl; R7 = H, C1-4 alkyl; R8 = e.g., 2-naphthyl, Ph, C1-6 alkoxy, (un)substituted C1-8 alkyl] or a pharmaceutically acceptable salt thereof, which are useful as prodrugs of inhibitors of trypsin-like proteases (no data), such as thrombin, and in particular in the treatment of conditions where inhibition of thrombin is required (e.g. thrombosis) or as anticoagulants, were prepd. For example, EtO2C-CH2-(R)Cgl-Aze-Pab-COOCH2CH:CH2 was prepd. via coupling of Me3CO2C-(R)Cgl-Aze-Pab-H with allyl chloroformate followed by Boc deprotection and coupling with Et bromoacetate. The title compds. were

all found to exhibit oral and/or parenteral bioavailability in rats as the active inhibitor HO2C-CH2-[redacted]Cgl-Aze-Pab-H, either as the f[redacted] acid and/or as one or more ester thereof.

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=> d his

     (FILE 'HOME' ENTERED AT 15:02:44 ON 27 MAY 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     15:03:08 ON 27 MAY 2003
L1         10904 S THROMBIN INHIBITOR
L2           514 S MELAGATRAN
L3         11005 S L1 OR L2
L4            68 S L3 (P) PRODRUG
L5       2981974 S KIT OR COMPOSITION
L6             0 S L4 (P) L5
L7        263691 S THROMBOSIS
L8           277 S THROMBOTIC CONDITION
L9        263784 S L7 OR L8
L10           13 S L9 (P) L4
L11            8 DUPLICATE REMOVE L10 (5 DUPLICATES REMOVED)

=> s l9 (p) surgery
L12       21370 L9 (P) SURGERY

=> s l11 (p) l12
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L83 (P) L74'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L85 (P) L75'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L87 (P) L76'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L89 (P) L77'
L13            3 L11 (P) L12

=> s l13 not l11
L14            0 L13 NOT L11

=> fd hsi
FD IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d his

     (FILE 'HOME' ENTERED AT 15:02:44 ON 27 MAY 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     15:03:08 ON 27 MAY 2003
L1         10904 S THROMBIN INHIBITOR
L2           514 S MELAGATRAN
L3         11005 S L1 OR L2
L4            68 S L3 (P) PRODRUG
L5       2981974 S KIT OR COMPOSITION
L6             0 S L4 (P) L5
L7        263691 S THROMBOSIS
L8           277 S THROMBOTIC CONDITION
L9        263784 S L7 OR L8
L10           13 S L9 (P) L4
L11            8 DUPLICATE REMOVE L10 (5 DUPLICATES REMOVED)
L12       21370 S L9 (P) SURGERY
L13           3 S L11 (P) L12
L14           0 S L13 NOT L11

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    34.82      35.03
```

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL S[redacted]ION
CA SUBSCRIBER PRICE	-3.26	[redacted].26

STN INTERNATIONAL LOGOFF AT 15:06:24 ON 27 MAY 2003